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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/847,945	05/02/2001	Neil P. Desai	ABI1460-3 (071243-1317)	6174

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EXAMINER	
GOLLAMUDI, SHARMILA S	

ART UNIT	PAPER NUMBER
1616	

DATE MAILED: 12/06/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/847,945	DESAI ET AL.	
	Examiner	Art Unit	
	Sharmila S. Gollamudi	1616	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *14 September 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,3-18 and 20-30* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,3-18 and 20-30* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Receipt of Amendments and Arguments filed on September 14, 2004 is acknowledged. Claims **1, 3-18, and 20-30** are pending in this application.

Priority

Acknowledgment is made of applicant's claim to priority back to June 27, 1997.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

The rejection of claims 1-16, 18-20, and 23-28 under 35 U.S.C. 112, first paragraph, for lack of enablement is withdrawn in view of the amendments of 9/14/04 specifying the drug.

New Rejections Necessitated by the Amendments of 9/14/04

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1, 3-18, and 20-30 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey

to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The amendment of 9/14/04 recites an "amorphous drug", which is not supported by the instant specification. It should be further noted that applicant has not cited any specific pages or lines where support may be found in the instant specification. If applicant contends there is support, the specific page and line in which support can be found is requested.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 1, 6-8, 18, and 20-30 are rejected under 35 U.S.C. 102(e) as being anticipated by Desai et al (5,916, 596).

Desai et al discloses an anticancer drug, specifically paclitaxel, coated with a protein for the treatment of cancer. Note that cancer is a type of hyperplasia. See abstract. The invention provides for small nanoparticles that are delivered in-vivo. See column 5, lines 53-55 and column 8, lines 17-22. Example 18 discloses intravenous therapy. The drug may be in a crystalline form or amorphous with amorphous preferred since it increases bioavailability. See column 7, lines 1-5 and claim 25. Example 14 discloses the treatment of tumors in an animal model by administering paclitaxel nanoparticles in tumor bearing mice. Lastly, example 30 discloses the reduced toxicity of the inventive protein coated drug nanoparticles.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 1, 6-8, 18, 20-30 are rejected under 35 U.S.C. 103(a) as being unpatentable over Grinstaff et al (5,498,421) in view of Westesen et al (6,197,349).

Grinstaff et al disclose encasing a water-insoluble biologically active agent in a polymeric shell (microparticles and nanoparticles) for in vivo delivery, most preferably IV. See abstract and column 1, lines 60-64. The delivery of the actives in the form of particles allows for targeting organs for treatment, increased stability of the insoluble active agent compared to simple emulsions, emulsifier-free system, a solubilizer-free system wherein allergic reactions are reduced, and the use of small doses. See column 7, lines 15-26. Diseases that can be targeted are cancers. See column 40-45. Note the term hyperplasia includes cancer. Grinstaff disclose proteins as suitable biocompatible materials for the formation of the polymeric shell. See column 8, lines 36-68. The active agents that may be incorporated into the polymeric shell are taxols and

camptothecin. See column 14, lines 1-6. Example 6 demonstrates the reduced toxicity of the drugs in the polymeric shells.

Grinstaff does not specify the drug form, i.e. instant amorphous form.

Westesen et al teach nanoparticles containing various drugs. See abstract. Westesen teaches the use of an amorphous form of the drug to provide for better solubility and bioavailability of the drug than utilizing a crystalline form. See column 5, lines 45-56.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to utilize an amorphous drug form in Grinstaff et al's nanoparticles. One would have been motivated to do so since Westesen teaches the use of an amorphous form for better solubility and bioavailability of poorly water-soluble drugs. Moreover, one would reasonably expect success by applying Westesen's teachings to Grinstaff since both are directed to poorly water-insoluble drugs.

Response to Arguments

Applicant's arguments with respect to claims 1, 3-18, and 20-30 have been considered but are moot in view of the new ground(s) of rejection.

Claims 1, 3-18, and 20-30 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kunz et al (5,733,925) of Westesen et al (6,197,349).

Kunz et al disclose methods for inhibiting stenosis following vascular trauma or disease, cancer, diseases resulting from hyperactivity or hyperplasia of somatic cells. Example 7 discloses smooth muscle proliferation in the neointima. Kunz teaches direct or targeted delivery of therapeutic agents to vascular smooth muscle cells. See column 1, lines 15-35. Inhibiting stenosis following angioplasty is contemplated. See column 3, lines 54-62. The dosage forms are

preferably in biodegradable microparticulates or nanoparticulates wherein the particles are formed of a polymer-containing matrix that biodegrades. Kunz et al teach conjugating the drug with a binding protein to target the cells and reduce toxicity. Example 7 notes the toxicity of a free drug versus a conjugated drug. See column 14, lines 25-33. Kunz et al disclose that the direct sustained release dosage form-binding protein or peptide conjugations may disrupt binding protein/peptide target cell recognition. Therefore, ligand sandwich attachment techniques are utilized. Such a technique involves the formation of a primary peptide or *protein shell* using a protein that does not bind to the target cell population. The binding protein/peptide is then bound to the primary peptide or protein shell to provide a particulate with functional binding protein/peptide. For example, the poly-lactic/glycolic acid particulates are reacted with avidin or streptavidin to form *protein-coated particulates*. Additionally, the binding protein/peptide may be partially entrapped in the particulate polymeric matrix upon formation of the particulate. See column 25, line 20 to column 26, line 40. Therapeutic agents such as taxol or analogs are preferred therapeutic agents that are designed to target the cell activity without killing the cell. Taxol is taken into the cell and stabilizes the cell from further dividing. See column 4, lines 40-45 and column 13, lines 24-27. Examples of dosages include .01 to 10 mg/kg per day. For prevention of restenosis following angioplasty or an intervention that contributes to the acute proliferation of smooth muscle cells, a pre-loading dose is given prior to or at the time of intervention with smaller chronic doses given two or three weeks after intervention. For example, a single dose may be administered about 24 hours prior to intervention, while multiple preloading doses may be administered daily for several days prior to intervention. See column

29, lines 10-15. Delivery of the active agents may be intravenous, intra-arterial (stents), or local delivery. See column 30, lines 56-65 and examples for stent deployment.

Kunz et al do not specify the drug form, i.e. instant amorphous form.

Westesen et al teach nanoparticles containing various drugs. See abstract. Westesen teaches the use of an amorphous form of the drug to provide for better solubility and bioavailability of the drug than utilizing a crystalline form. See column 5, lines 45-56.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to utilize an amorphous drug form in Kunz et al's nanoparticles. One would have been motivated to do so since Westesen teaches the use of an amorphous form for better solubility and bioavailability of poorly water-soluble drugs. Moreover, one would reasonably expect success by applying Westesen's teachings to Kunz since both are directed to poorly water-insoluble drugs.

Response to Arguments

Applicant's arguments with respect to claims 1, 3-18, and 20-30 have been considered but are moot in view of the new ground(s) of rejection. However, since the examiner has retained Kunz et al has the primary reference, the main argument by the applicant will be addressed.

Applicant argues that Kunz does not teach a physically coated drug and rather teaches a complex process of protein conjugation.

Applicant's arguments have been fully considered but they are not persuasive. The examiner points to column 25 and 26, wherein Kunz teaches different methods of making the micro and nanoparticulates. The examiner particularly points to column 26, line 2 wherein "protein coated particulates" are taught.

Conclusion

All claims remain rejected at this time.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sharmila S. Gollamudi whose telephone number is 571-272-0614. The examiner can normally be reached on M-F (8:00-5:30), alternate Fridays off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Kunz can be reached on 571-272-0887. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Sharmila S. Gollamudi
Examiner
Art Unit 1616

SSG

MICHAEL G. HARTLEY
PRIMARY EXAMINER